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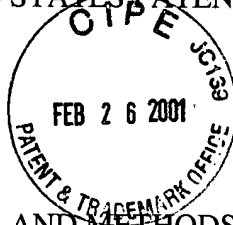
IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of
SMITH et al.

Serial No. 09/662,462

Filed: September 15, 2000

For: NUCLEIC ACID PROBES AND METHODS FOR
DETECTING CLINICALLY IMPORTANT
FUNGAL PATHOGENS



Atty. Ref.: 2551-49

Group: 1655

Examiner: Goldberg

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February 26, 2000

Assistant Commissioner for Patents
Washington, DC 20231

RESPONSE

Sir:

Responsive to the Office Action dated January 25, 2001, the applicants elect, with traverse, the subject matter of Group I for further prosecution in the above.

The restriction requirement should be withdrawn however as all of the claimed subject matter has been classified in Class 435, Subclass 6, indicating the subject matter of the Examiner's allegedly separately patentable Groups are, in fact, recognized as not requiring a separate field of search. That is, while the Examiner may show claims are distinct based on a separate classification (i.e., thus showing distinct subject matter has obtained recognition in the art is a separate subject for inventive effort and that a separate field of search is required (MPEP §808.02)) the converse should also be true. The Examiner's indication that there is only one Group of distinct subject matter based on a separate classification is evidence that there is, in fact, one distinct invention which is being claimed.

In addition, the Examiner is urged to appreciate that if the applicants are required to divide the subject matter in to 13 "inventions", as required by the Examiner, the applicants rights to the inventive concept of this application, i.e. the simultaneous detection and identification of the different fungal species in one single assay, may be diminished. The presently claimed

invention is directed, in part, to the use of a specific set of primers and probes. The applicants respectfully submit that the fungi *Aspergillus*, *Candida* and *Cryptococcus* are responsible for deep mycoses and pose tremendous challenges for clinicians. Moreover, methods for simultaneous detection and differentiation of a wide variety of fungal species with clinical importance have, prior to the present invention, not been described.

The Examiner's requirement for restriction inappropriately divides the subject matter, to the potential detriment of any clinical and/or commercial advantage and applicability of the current invention. In the event the Examiner refuses to withdraw the restrictions requirement, consideration and grant of the attached Alternate Rule 181 Petition, and withdrawal of the restriction requirement are requested.

In the event the restriction requirement is not withdrawn, and the attached Alternate Rule 181 Petition is not granted, the applicants further request consideration of the following alternate restrictions:

The applicants submit it is illogical to divide the invention corresponding to detection methods applicable for the 7 different *Candida* species. *Candida* infections, indicated by the term 'candidoses', are one of the most common invasive fungal infections. It has been recognized that different *Candida* species and subspecies differ in their ability to cause disease, so it should be of clinical importance to identify and type *Candida* isolates. Efficient treatment regimens of fungal diseases require a correct identification of the fungus at the species level.

Thus the grouping of the methods related to detection of the different *Candida* species enables the detection and differentiation of closely related organisms belonging to the same genus in one single assay. With the use of a "fungal universal primer pair" it is possible to amplify the ITS region of most, if not all, fungal species. In addition, all probes are designed

such that they are functional under identical hybridization conditions, thus allowing any possible combination.

Similar arguments apply for the *Aspergillus* species, but moreover, it is of particular interest to further combine the groups relating to resp. different *Candida* species and *Aspergillus* species, as described by the Examiner (Groups I-XI). There is a clear link between the two organisms/diseases since candidiasis and aspergillosis account for between 80% and 90% of systemic fungal infections in immuno-compromised patients. In patients with positive fungus cultures, *Aspergillus* species are the second most common isolate after *Candida* species. Since these fungi are most common in deep mycoses it should be important to have detection methods which make it possible to identify the different species. It is known that efficient treatment regimens of fungal diseases require a correct identification of the fungus at the species level.

Based on the above considerations, the applicants submit that, if the restriction requirement is maintained and the attached Alternate Petition is denied, the restriction requirement should be restated to include only the following 3 Groups, i.e.

Group IA related to a combined detection and identification method of *Candida* species and *Aspergillus* species;

Group IIA related to detection and identification of *Cryptococcus neoformans*; and

Group IIIA related to detection and identification of *Pneumocystis carinii*.

In the event the Examiner restates the restriction requirement with the above-noted 3 Groups, the applicants elect, with traverse, the subject matter of Group IA.

In the event the restriction requirement is maintained and the attached Alternate Petition denied and the Examiner believes the above three-way restriction requirement is inappropriate, the Examiner is requested to restate the restriction requirement to include the following 4

Groups:

Group IB related to methods for detection and identification of the different *Candida* species.

Group IIB related to methods for detection and identification of the different *Aspergillus* species.

Group IIIB related to methods for detection and identification of *Cryptococcus neoformans*.

Group IVB related to methods for detection and identification of *Pneumocystis carinii*.

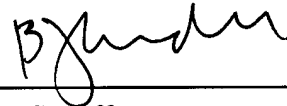
In the event the Examiner restates the restriction requirement with the above-noted 4 Groups, the applicants elect, with traverse, the subject matter of Group IB.

Traversal is based on the fact that the Examiner has indicated that the claims are defined by a single Class and Subclass, such that the subject matter of the claims has not obtained recognition in the art as being directed to subject matter requiring separate inventive effort. Search of all the claimed subject matter would not therefore be an undue burden on the Examiner.

Withdrawal of the restriction requirement and an early and favorable Action on the merits of all the claimed subject matter are requested.

Respectfully submitted,

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